## REMARKS

With the proposed claim amendments submitted herein, claims 1-3, 5-6, 15-20 and 35-37 are currently pending in the instant application. Claims 4, 10-11, 38 and 39 have been cancelled, and Applicant reserves the right to prosecute that subject matter, as well as the originally presented claims, in continuing applications.

Claims 1-3, 35 and 37 have been amended to recite an autoimmune or inflammatory disorder "selected from the group consisting of psoriasis, Type I diabetes, multiple sclerosis, rheumatoid arthritis and atherosclerosis." Support for this amendment can be found throughout the specification and in the claims as originally filed. For example, support for this amendment can be found at least at page 20, lines 4-8, and at page 20, lines 28-30, and in original claims 9 and 11. Claims 1-3 and 5 have been amended to recite methods directed to humans. Support for this amendment can be found throughout the specification and in the claims as originally filed. Specifically, support for this amendment can be found at least at page 18, lines 28-29 and in original claim 4. Finally, claim 18 has been amended to correct a typographical error. Accordingly, no new matter has been added.

Applicant notes with appreciation that the Examiner has withdrawn the objections to claims 7, 21, 26, 27, 29 and 32, as well as the rejections under 35 U.S.C. § 112, first and second paragraphs, in light of the amendments filed on December 12, 2002.

## I. DOUBLE PATENTING

### 1. Provisional rejection under statutory-type (35 U.S.C. §101) double patenting

U.S. Application No. 09/960,471

The Examiner maintains the provisional statutory-type double patenting rejection of claims 1-6, 10-11, 15-20 and 35-37 as claiming the same invention as claims 1-7, 9-11, 13-16, 18, 20-26 and 31-33 of copending U.S. Application No. 09/960,471. According to the Examiner, the "CD40-mediated anti-immuno-inflammatory effect in a mammal is inherently present in the method of administering a statin compound to the mammal."

Applicant traverses the Examiner's assertion that the conflicting claims are directed to "the same invention." In copending U.S. Application No. 09/960,471, Applicant has cancelled claims 1-3, 7-10, 13-15, 27-28, and 31-92 in response to a Restriction Requirement dated

December 17, 2002. A copy of the Amendment canceling these claims has been attached hereto as Exhibit A. Claim 4, the remaining independent claim in copending U.S. Application No. 09/960,471, is directed to a "method to achieve CD40-mediated anti immuno-inflammatory effect in a mammal in need of such treatment, which comprises administering to the mammal at least one statin, or a functionally or structurally equivalent molecule, in an amount effective to modulate CD40 expression."

In contrast, the independent claims pending in the present application (*i.e.*, claims 1-3) are directed to methods to achieve MHC class II-mediated immunomodulation, immunosuppression or anti-inflammatory effect in a mammal with an MHC class II-mediated inflammatory or autoimmune disorder characterized by interferon gamma inducible class II transactivator (CIITA) expression.

These inventions recited by the claims of the present application and the pending claims in U.S. Application No. 09/960,471 are patentably distinct. In fact, the Examiner, who is also directing prosecution of U.S. Application No. 09/960,471, has already acknowledged that these inventions are patentably distinct. In a Restriction Requirement dated December 17, 2002, Examiner Hui stated:

> Inventions I-IX are unrelated ... The inventions of Group I, IV, and VII function to achieve MHC Class II mediated immunomodulation in different patient populations ... The inventions of Group II, V, and VIII function to achieve MHC Class II mediated anti-inflammatory effect in different patient populations ... The inventions of Group III, VI, and IX function to achieve CD40-mediated and anti-immunoinflammation in different populations. (Office Action, pp. 6-7).

In this Restriction Requirement, the Examiner further characterized the inventions in each group of claims as "distinct" and having "acquired a separate status in the art because of their recognized divergent subject matter." (December 17, 2002 Restriction Requirement, p. 8). As the inventions recited in the instant application and in copending U.S. Application No. 09/960,471 are unrelated and distinct, Applicant requests that the Examiner withdraw this double-patenting rejection.

U.S. Application Nos. 10/056,608; 10/056,288; 10/056,645; 10/056,133; 10/056,606; and 10/056,646

The Examiner also maintains the provisional statutory-type double patenting rejection of claims 2-6, 10-11, 15-20 and 35-37 in light of claims 2-7, 9-11, 13-16, 18, 20-26 and 31-33 of copending U.S. Application Nos. 10/056,608; 10/056,288; 10/056,645; 10/056,133 and 10/056,606, as well as the provisional statutory-type double patenting rejection of claims 1-6, 10-11, 15-20 and 35-37 in light of claims 1-7, 9-11, 13-16, 18, 20-26 and 31-33 of copending U.S. Application No. 10/056,646. According to the Examiner, "the CD40-mediated anti-immuno-inflammatory effect in a mammal is inherently present in the method of administering a statin compound to the mammal."

Applicant notes that claims 1-7, 9-11, 13-16, 18, 20-26 and 31-33 have been cancelled in each of the cited copending applications (*i.e.*, U.S. Application Nos. 10/056,608; 10/056,288; 10/056,645; 10/056,133; 10/056,606; and 10/056,646). In each of these cited applications, claims 1-93 were cancelled in the "Request for Filing a Continuing Utility Application Under 37 C.F.R. §1.53(b)" and a Preliminary Amendment submitted therewith. Copies of the documents in which claims 1-93 have been cancelled in U.S. Application Nos. 10/056,645; 10/056,646; 10/056,606; 10/056,133; 10/056,608; and 10/056,288 have been attached hereto as Exhibits B-G.

As the claims cited by the Examiner have been cancelled, these provisional statutory-type double patenting rejections have been rendered moot. Accordingly, Applicant requests that the Examiner withdraw these rejections.

**2. Provisional rejection under nonstatutory-type (obviousness-type) double patenting**

U.S. Application Nos. 10/056,608; 10/056,288; 10/056,645; 10/056,133; and 10/056,606

The Examiner has maintained the provisional rejection of claims 1-6, 10-11, 15-20 and 35-37 under the judicially created doctrine of obviousness-type double patenting in light of claims 36-48- and 76-93 of copending U.S. Application Nos. 10/056,608; 10/056,288; 10/056,645; 10/056,133; and 10/056,606. As discussed above in connection with the provisional rejection of these claims under statutory-type double patenting, claims 1-93 have been cancelled in each of the cited copending applications. Copies of the documents in which these claims have been cancelled in copending U.S. Application Nos. 10/056,608; 10/056,288; 10/056,645;

10/056,133; and 10/056,606 have been attached hereto as Exhibits B and D-G. Thus, these provisional non-statutory double patenting rejections have been rendered moot, and Applicant requests that the Examiner withdraw these rejections.

U.S. Application No. 10/056,646

The Examiner has also maintained the provisional rejection of claims 1-6, 10-11, 15-20 and 35-37 under the judicially created doctrine of obviousness-type double patenting in light of claims 36-48- and 76-106 in copending U.S. Application No. 10/056,646. Once again, Applicant notes that claims 1-93 of copending U.S. Application No. 10/056,646 have been cancelled, thereby rendering the rejection moot with regard to claims 76-93. A copy of the documents in which claims 1-93 have been cancelled in U.S. Application 10/056,646 has been attached hereto as Exhibit C. Accordingly, the rejection has been rendered moot with regard to claims 1-93, and Applicant requests that the Examiner withdraw the rejection for these claims.

With regard to the provisional rejection of the pending claims in light of claims 94-106 of copending U.S. Application No. 10/056,646, Applicant herein elects to prosecute 1-6, 10-11, 15-20 and 35-37 of the present application. Accordingly, Applicant will cancel claims 94-106 of U.S. Application 10/056,646. Applicant, therefore, requests that the Examiner withdraw this rejection in the present application.

## II. CLAIM REJECTIONS

### 1. Rejection of claims 1-6, 10-11, 15-20 and 35-37 under 35 U.S.C. § 112, second paragraph

Claims 1-6, 10, 11, 15-20 and 35-37 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. In particular, the Examiner has asserted that "it is not clear what conditions would be considered 'an MHC Class II-mediated inflammatory or autoimmune disorder characterized by IFN-γ inducible Class II transactivator expression," and furthermore, "it is also not clear what mammal will be encompassed by the claims."

Independent claims 1-3, 35 and 37 have been amended to recite methods that are directed to autoimmune or inflammatory disorders "selected from the group consisting of psoriasis, Type I diabetes, multiple sclerosis, rheumatoid arthritis and atherosclerosis." Thus, the claims have been amended to recite the specific "MHC Class II-mediated inflammatory or autoimmune

[disorders] characterized by IFN-γ inducible Class II transactivator expression" encompassed by the claimed invention. Therefore, Applicant requests that the Examiner withdraw this rejection.

In addition, independent claims 1-3 have been amended herein to recite methods that are directed to achieving MHC Class II-mediated immunomodulation, immunosuppression or anti-inflammatory effect in humans. Accordingly, this rejection under 35 U.S.C. §112, second paragraph has been rendered moot, and Applicant requests that the Examiner withdraw this rejection as well.

**2. Rejection of claims 1-3, 6, 11, 15 and 20 under 35 U.S.C. § 102(e)**

Claims 1-3, 6, 11, 15 and 20 stand rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,403,637 B1 ("Partridge"). In particular, the Examiner has asserted that Partridge teaches a method of treating arthritis in a mammal comprising administering an effective amount of atorvastatin to the mammal. According to the Examiner, "administering compounds inherently possessing a protective utility anticipates claims directed to such protective use," and Applicant has failed to "distance the proffered claims from the anticipated utility." (Office Action, p. 8-9). The Examiner concludes that Partridge is a U.S. patent that claims the rejected claims, and therefore, "this reference can only be overcome by establishing priority of invention through interference proceedings."

Applicant traverses, as the claims of the present invention have an invention date prior to the effective filing date of Partridge. The earlier invention date for the pending claims has been previously established by the Declaration Under 37 C.F.R. §1.131 of Francois Mach, which was submitted by Applicant on December 2, 2002. The purpose of this Rule 131 Declaration was to "swear behind" Partridge to demonstrate that this reference is unavailable as prior art. Applicant did not submit this Rule 131 Declaration of Francois Mach in an effort to prove an earlier invention date for the subject matter disclosed by Partridge. Rather, the Declaration was submitted to establish an earlier invention date for Applicant's own claimed subject matter – a patentably distinct invention. Accordingly, Applicant contends that the Partridge reference is unavailable as prior art, and this rejection should be withdrawn.

Even if Partridge were available as prior art, Partridge does not anticipate the pending claims. Independent claims 1-3 have been amended to recite methods for achieving MHC Class II-mediated immunomodulation, immunosuppression or anti-inflammatory effect in a human

with an MHC Class II-mediated inflammatory or autoimmune disorder characterized by IFN-γ inducible Class II transactivator expression, wherein the inflammatory or autoimmune disorder is selected from the group consisting of "psoriasis, Type I diabetes, multiple sclerosis, rheumatoid arthritis and atherosclerosis."

Partridge, in contrast, is directed to methods of administering a statin to treat conditions like osteoarthritis, which are characterized by excessive amounts of matrix metalloproteinases. In fact, the examples and actual test data provided by Partridge are limited to the treatment of osteoarthritis in particular. (*See e.g.*, Breaker, Example 3, at col. 24, line 30).

The pending claims, however, do not recite osteoarthritis. Rather, these claims are directed to rheumatoid arthritis and other MHC Class II-mediated autoimmune or inflammatory disorders. One of ordinary skill in the art would readily appreciate that rheumatoid arthritis is a very different disease from osteoarthritis, and patients suffering from osteoarthritis do not have the disease characteristics recited by the pending claims. In particular, osteoarthritis patients do not have an MHC Class II-mediated inflammatory or autoimmune disorder characterized by IFN-γ inducible Class II transactivator expression.

To demonstrate the differences between osteoarthritis and rheumatoid arthritis, Applicant submits herewith a Declaration Under 37 C.F.R. §1.132 of Francois Mach, the named inventor of the present application. Osteoarthritis is a known degenerative joint condition that is characterized by the progressive deterioration of articular cartilage at a joint surface and by the presence of excessive amounts of matrix metalloproteinases. (*See* Mach Decl., ¶ 4). One of ordinary skill in the art would appreciate that osteoarthritis is not an MHC Class II-mediated autoimmune or inflammatory disorder. (*See* Mach Decl., ¶ 5). Rheumatoid arthritis, in contrast, is a known autoimmune disorder characterized by persistent, chronic inflammation of the synovium. (*See* Mach Decl., ¶ 6). Those skilled in the art would understand that development of rheumatoid arthritis is associated with the presence of the MHC Class II gene product HLA-DLR4, and therefore, rheumatoid arthritis is a known MHC Class II-mediated autoimmune disorder. (*See* Mach Decl., ¶ 7).

Thus, osteoarthritis patients do not have the claimed disease characteristics recited by claims 1-3 (and their respective dependent claims), because people suffering from osteoarthritis do not have an MHC Class II-mediated inflammatory or autoimmune disorder, characterized by IFN-γ inducible Class II transactivator expression and selected from the group consisting of

psoriasis, Type I diabetes, multiple sclerosis, rheumatoid arthritis and atherosclerosis. Accordingly, the subjects treating using the Partridge methods of inactivating a matrix metalloproteinase are different from the patients treated according to the methods disclosed by Applicant.

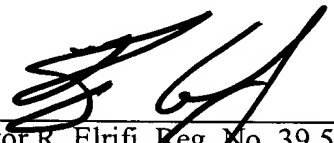
Moreover, one of ordinary skill in the art would not expect to use the claimed methods in the treatment of a disease that is not an MHC Class II-mediated autoimmune or inflammatory disorder. In the present invention, statins are used as novel immunomodulators, immunosuppressors and anti-inflammatory agents in MHC Class II-mediated inflammatory or autoimmune disorders, because statins repress induction of MHC Class II molecules and subsequent T cell activation. (*See* Mach Decl., ¶ 9). Thus, one would not expect to use the claimed methods to treat osteoarthritis or other disorders that are not associated with MHC Class II expression.

Accordingly, Partridge fails to teach or suggest the claimed methods for achieving MHC Class II-mediated immunomodulation, immunosuppression or anti-inflammatory effect in a human. Claims 1-3, 5, 11, 15 and 20 are, therefore, not anticipated, and Applicant requests that the Examiner withdraw this rejection.

## CONCLUSION

On the basis of the foregoing amendments and arguments, Applicant submits that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



Ivor R. Elrifi, Reg. No. 39,529
Attorney for Applicant
MINTZ, LEVIN, COHN, FERRIS,
GLOVSKY and POPEO, P.C.
One Financial Center
Boston, Massachusetts 02111
Tel: (617) 542-6000
Fax: (617) 542-2241

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*Version With Markings to Show Changes*

***In the Claims:***

Claims 4, 10-11, 38 and 39 have been cancelled.

Claims 1-3, 18, 35 and 37 have been amended.

1. (Currently Amended) A method to achieve MHC-class II mediated immunomodulation in a [mammal] human with an MHC Class II-mediated inflammatory or autoimmune disorder characterized by IFN-γ inducible Class II transactivator expression, the method comprising administering to said mammal at least one statin selected from the group consisting of compactin, atorvastatin, lovastatin, pravastatin, fluvastatin, mevastatin, cerivastatin, and simvastatin, in an amount effective to modulate MHC class II expression in said mammal, wherein the an MHC Class II-mediated inflammatory or autoimmune disorder characterized by IFN-γ inducible Class II transactivator expression is selected from the group consisting of psoriasis, Type I diabetes, multiple sclerosis, rheumatoid arthritis and atherosclerosis.

2. (Currently Amended) A method to achieve MHC-class II mediated immunosuppression in a [mammal] human with an MHC Class II-mediated inflammatory or autoimmune disorder characterized by IFN-γ inducible Class II transactivator expression, the method comprising administering to said mammal at least one statin selected from the group consisting of compactin, atorvastatin, lovastatin, pravastatin, fluvastatin, mevastatin, cerivastatin, and simvastatin, in an amount effective to suppress MHC class II expression in said mammal, wherein the an MHC Class II-mediated inflammatory or autoimmune disorder characterized by IFN-γ inducible Class II transactivator expression is selected from the group consisting of psoriasis, Type I diabetes, multiple sclerosis, rheumatoid arthritis and atherosclerosis.

3. (Currently Amended) A method to achieve MHC-class II mediated anti-inflammatory effect in a [mammal] human with an MHC Class II-mediated inflammatory or autoimmune disorder characterized by IFN-γ inducible Class II transactivator expression, the method comprising administering to said mammal at least one statin selected from the group consisting of compactin, atorvastatin, lovastatin, pravastatin, fluvastatin, mevastatin, cerivastatin, and

simvastatin, in an amount effective to suppress MHC class II expression in said mammal, wherein the an MHC Class II-mediated inflammatory or autoimmune disorder characterized by IFN-γ inducible Class II transactivator expression is selected from the group consisting of psoriasis, Type I diabetes, multiple sclerosis, rheumatoid arthritis and atherosclerosis.

4. (Cancelled)

5. (Currently Amended) The method of claims 1, 2 or 3, wherein said [mammal] human does not suffer from hypercholesterolaemia.

10. (Cancelled)

11. (Cancelled)

18. (Currently Amended) The method of claims 1, 2 or 3, wherein said administration comprises intralesional, intraperitoneal, intramuscular or intravenous injection; infusion; or topical, nasal, oral, ocular or [otic] optic delivery.

35. (Currently Amended) A method of treating a patient afflicted with an autoimmune disease characterized by IFN-γ inducible Class II transactivator expression, comprising administering to said patient a compound that inhibits 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA reductase) in an amount effective to treat said disease, wherein the autoimmune disorder characterized by IFN-γ inducible Class II transactivator expression is selected from the group consisting of psoriasis, Type I diabetes, multiple sclerosis, rheumatoid arthritis and atherosclerosis.

37. (Currently Amended) A method of treating a patient suffering from an autoimmune disease or condition characterized by IFN-γ inducible Class II transactivator expression comprising:

administering to said patient at least one compound, capable of measurable HMG-CoA reductase inhibition and inhibition of MHC Class II expression in said patient, in an amount

effective to treat such autoimmune disease or condition, wherein the autoimmune disease or condition characterized by IFN-γ inducible Class II transactivator expression is selected from the group consisting of psoriasis, Type I diabetes, multiple sclerosis, rheumatoid arthritis and atherosclerosis.

38. (Cancelled)

39. (Cancelled)